This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

Claims 1-49(canceled).

50(currently amended). An assay method for the determination of holo-TranscobalaminII (holo-TCII) in a body sample, comprising contacting a cell free sample of a body fluid with an immobilized cobalamin or an analogue or fragment thereof which selectively binds the apo-forms of TCII and haptocorrin (HC) in said sample over the holo-forms thereof, subsequently contacting said sample which has been contacted with the immobilized cobalamin or analogue or fragment thereof, with a specific binding ligand for TCII or holo-TCII, separating a ligand bound fraction from a non-ligand bound fraction and measuring the TCII ~~or cobalamin~~ content of said ligand bound fraction to determine the quantity of holo-TCII in the body sample being assayed, wherein the binding of said apo-TCII to said immobilised cobalamin or analogue or fragment thereof is followed by removal of said apo-TCII or renders said apo-TCII unable to bind to said specific binding ligand for TCII or holo-TCII.

51(previously presented). An assay method as claimed in claim 50 wherein the separation of said ligand bound fraction from said non-ligand bound fraction is so performed that the holo-TCII concentration is increased by at least 3-fold.

52(previously presented). An assay method as claimed in claim 50 wherein said assay is capable of detecting holo-TCII at a concentration as low as 9 pM.

53(previously presented). An assay method as claimed in claim 50 wherein said specific binding ligand is a ligand selected from the group consisting of a polyclonal antibody, a monoclonal antibody, and an antibody fragment.

54(previously presented). An assay method as claimed in claim 50 wherein said specific binding ligand exhibits a high degree of selectivity and specificity towards TCII and exhibits low affinity towards other transcobalamin proteins, in either apo or holo form, or any other cobalamin-binding protein.

55(cancelled).

56(cancelled).

57(cancelled).

58(previously presented). An assay method as claimed in claim 50 wherein said specific binding ligand binds holo-TCII with an affinity constant of at least $10^{9}M^{-1}$.

59(previously presented). An assay method as claimed in claim 50 wherein said specific binding ligand binds holo-TCII with an affinity constant of greater than $10^{11}M^{-1}$.

60(previously presented). An assay method as claimed in claim 50 wherein the degree of cross-reactivity of said specific binding ligand with HC is between 0.1% and 1%.

61(previously presented). An assay method as claimed in claim 50 wherein the degree of cross-reactivity of said specific binding ligand with HC is less than 0.1%.

62(previously presented). An assay method as claimed in claim 50 wherein said sample which has been contacted with the immobilized cobalamin or analogue or fragment thereof is further contacted with a solid phase support having immobilized thereon said specific binding ligand and to which is bound a labelled ligand recognizing the same binding sites on the immobilized specific binding ligand as holo-TCII, whereby holo-TCII in said sample competes with said bound labelled ligand for said binding sites such that after equilibration of the system there is a directly proportional relationship between the amount of labelled ligand displaced from said solid phase support and detectable in solution and the amount of holo-TCII present in the original sample; said labelled ligand being detected directly or indirectly as the amount of labelled ligand bound or not bound to said solid phase support as appropriate.

63(previously presented). An assay method as claimed in claim 50 wherein said sample which has been contacted with the immobilised cobalamin or analogue or fragment thereof is further contacted with a solid phase support having holo-TCII immobilised thereon and with a labeled non-immobilised holo-TCII specific binding ligand, whereby free holo-TCII in the sample and immobilised holo-TCII compete for binding to the labelled non-immobilised ligand; and determination of the labelled ligand bound to the solid phase support or remaining in solution allows determination of the holo-TCII concentration.

64(previously presented). An assay method as claimed in claim 50 wherein said sample which has been contacted with the immobilised cobalamin or analogue or fragment thereof is further contacted with labeled holo-TCII and an immobilised ligand therefor whereby labelled and non-labeled holo-TCII compete for binding to the immobilised ligand and after equilibrium is reached, the amount of labeled holo-TCII bound to the immobilised ligand is indirectly proportional to the amount of holo-TCII in the sample.

65(previously amended). An assay method as claimed in claim 50 wherein said body sample is a sample selected from the group consisting of seminal fluid, cerebro-spinal fluid, amniotic fluid and a blood derived sample.

66(previously presented). An assay as claimed in claim 65 wherein said blood derived sample is serum or plasma.

67(previously presented). An assay method as claimed in claim 50 wherein said bound fraction is separated from said unbound fraction by precipitation, centrifugation, filtration or chromatographic methods.

68(previously presented). An assay method as claimed in claim 50 wherein said ligand is labelled with a signal forming label which may be determined by luminescence, chemiluminescence, colorimetric assessment, fluorescence, radioactivity or by enzymic activity.

69(previously presented). An assay method as claimed in claim 50 in which assay calibration is effected using a holo-TCII standard.

70(previously presented). An assay as claimed in claim 69 wherein said standard is human, native or recombinant holo-TCII.

Claims 71-72(canceled).

73 (new). An assay method for the determination of holo-TranscobalaminII (holo-TCII) in a body sample, comprising contacting a cell free sample of a body fluid with an immobilized cobalamin or an analogue or fragment thereof which selectively binds the apo-forms of TCII and haptocorrin (HC) in said sample over the holo-forms thereof, subsequently contacting said sample which has been contacted with the

immobilized cobalamin or analogue or fragment thereof, with a specific binding ligand for TCII or holo-TCII, separating a ligand bound fraction from a non-ligand bound fraction and measuring the cobalamin content of said ligand bound fraction to determine the quantity of holo-TCII in the body sample being assayed, wherein the binding of said apo-TCII to said immobilised cobalamin or analogue or fragment thereof is followed by removal of said apo-TCII or renders said apo-TCII unable to bind to said specific binding ligand for TCII or holo-TCII.

74(new). An assay method as claimed in claim 73 wherein cobalamin in said ligand bound fraction is released from the holo TCII molecules therein by changing the temperature or the pH of the surrounding medium.

75(new). An assay method as claimed in claim 73 wherein said released cobalamin is determined by a competition assay performed by contacting an immobilised binding partner for cobalamin with the released cobalamin of the sample in the presence of labeled cobalamin analogue which competes with the released cobalamin for binding to the immobilised binding partner.